



Sequence Listing

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LOWMAN, HENRY B.
MULLER, YVES

<120> ANTIBODY VARIANTS

<130> P1469R1C1

<140> US 10/624,153

<141> 2003-07-21

<150> US 09/440,781

<151> 1999-11-16

<150> US 60/108,945

<151> 1998-11-18

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 Gly Tyr Asp Phe Thr Asn Tyr Gly Ile Asn
 1 5 10
 <210> 20
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 Gly Tyr Asp Tyr Thr Asn Tyr Gly Ile Asn
 1 5 10
 <210> 21
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 Gly Tyr Asp Trp Thr Asn Tyr Gly Ile Asn
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 Trp Ile Asn Thr Trp Thr Gly Glu Pro Thr Tyr Ala Ala
 1 5 10

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 Tyr Pro His Tyr Tyr Val Gly Glu Thr Ser Ser His Trp Tyr Phe
 1 5 10 15
 Asp Val

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Tyr Pro His Tyr Tyr Ala Arg Asp Arg Ser Ser His Trp Tyr Phe
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Asp Val

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Tyr Pro His Tyr Tyr Glu Arg Asp Gly Lys Ser Ser His Trp Tyr
1 5 10 15

Phe Asp Val

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Tyr Pro His Tyr Tyr Arg Asn Glu Lys Ser Ser His Trp Tyr Phe
1 5 10 15

Asp Val

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 1 5 10 15

Asp Val

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 Tyr Pro His Tyr Tyr Gln Arg Asp Arg Ser Ser His Trp Tyr Phe
 1 5 10 15

Asp Val

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 Tyr Pro His Tyr Tyr Gly Asn His Arg Ser Ser His Trp Tyr Phe
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Asp Val

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Tyr	Pro	His	Tyr	Tyr	Gln	Asp	Glu	Lys	Ser	Ser	His	Trp	Tyr	Phe
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Asp Val

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Asp Val

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<400> 43
 Tyr Pro His Tyr Tyr His Thr Arg Gly Gly Ser Ser His Trp Tyr
 1 5 10 15

Phe Asp Val

<210> 44
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 Asp Val

 <210> 45
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 1 5 10 15
 Asp Val

 <210> 46
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 <400> 46
 Tyr Pro His Tyr Tyr Arg Asn Glu Arg Ser Ser His Trp Tyr Phe
 1 5 10 15
 Asp Val

 <210> 47
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Asp Val

<210> 48

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Tyr	Pro	His	Tyr	Tyr	Leu	Ala	Asp	Arg	Ser	Ser	His	Trp	Tyr	Phe
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Asp Val

<210> 49

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<222> 1-17

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Tyr	Pro	His	Tyr	Tyr	Val	Asn	Glu	Arg	Ser	Ser	His	Trp	Tyr	Phe
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Asp Val

<210> 50

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Tyr Pro His Tyr Tyr Leu Lys Asp Lys Ser Ser His Trp Tyr Phe
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Asp Val

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Tyr Pro His Tyr Tyr Leu Lys Asp Gly Arg Ser Ser His Trp Tyr
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Phe Asp Val

<210> 52
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Tyr Pro His Tyr Tyr Glu Arg Asp Gly Arg Ser Ser His Trp Tyr
1 5 10 15

Phe Asp Val

<210> 53
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 Tyr Pro His Tyr Tyr Leu Arg Asp Gly Arg Ser Ser His Trp Tyr
 1 5 10 15

 Phe Asp Val

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 1 5 10 15

 Val

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 Asp Val

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Phe Asp Val

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Phe Asp Val

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Tyr Pro His Tyr Tyr Glu Lys Gln Arg Lys Ser His Trp Tyr Phe
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Asp Val

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Tyr Pro His Tyr Tyr Ser His Gln Lys Arg Ser His Trp Tyr Phe
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Asp Val

<210> 61
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Asp Val

<210> 62
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Asp Val

<210> 63

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<222> 1-17

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Tyr	Pro	His	Tyr	Tyr	Ser	Val	Glu	Gly	Gly	Ser	His	Trp	Tyr	Phe
1				5					10					15

Asp Val

<210> 64

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<222> 1-17

<223> variant CDR sequence

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1				5					10					15

Asp Val

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<222> 1-17

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1 5 10 15

Asp Val

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1 5 10 15

Asp Val

<210> 67
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Tyr Pro His Tyr Tyr Ser Asn Glu Arg Lys Ser His Trp Tyr Phe
1 5 10 15

Asp Val

<210> 68
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Tyr Pro His Tyr Tyr Arg Gly Asp Arg Lys Ser His Trp Tyr Phe
1 5 10 15

Asp Val

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Tyr Pro His Tyr Tyr Ser Asp Glu Lys Lys Ser His Trp Tyr Phe
1 5 10 15

Asp Val

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Tyr Pro His Tyr Tyr Arg Ser Gln Arg Lys Ser His Trp Tyr Phe
1 5 10 15

Asp Val

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Tyr Pro His Tyr Tyr Ala Trp Arg Asp Arg Arg Ser His Trp Tyr
 1 5 10 15

Phe Asp Val

<210> 72
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 Tyr Pro His Tyr Tyr Ala Asn Arg Glu Arg Lys Ser His Trp Tyr
 1 5 10 15

Phe Asp Val

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 <223> variant CDR sequence

<400> 73
 Tyr Pro His Tyr Tyr Val Asn Asp Lys Thr Ser His Trp Tyr Phe
 1 5 10 15

Asp Val

<210> 74
 <211> 17
 <212> PRT
 <213> artificial sequence

<220>
 <223> sequence is synthesized

<220>
 <221> artificial
 <222> 1-17
 <223> variant CDR sequence

<400> 74
Tyr Pro His Tyr Tyr Val Glu Glu Thr Glu Ser His Trp Tyr Phe
1 5 10 15

Asp Val

<210> 75
<211> 17
<212> PRT
<213> artificial sequence

<220>
<223> sequence is synthesized

<220>
<221> artificial
<222> 1-17
<223> variant CDR sequence

<400> 75
Tyr Pro His Tyr Tyr Glu Lys Glu Arg Lys Ser His Trp Tyr Phe
1 5 10 15

Asp Val

<210> 76
<211> 17
<212> PRT
<213> artificial sequence

<220>
<223> sequence is synthesized

<220>
<221> artificial
<222> 1-17
<223> variant CDR sequence

<400> 76
Tyr Pro His Tyr Tyr Ser His Glu Arg Val Ser His Trp Tyr Phe
1 5 10 15

Asp Val

<210> 77
<211> 17
<212> PRT
<213> artificial sequence

<220>
<223> sequence is synthesized

<220>
<221> artificial
<222> 1-17
<223> variant CDR sequence

<400> 77

Tyr Pro His Tyr Tyr Arg Asp Glu Arg Glu Ser His Trp Tyr Phe
 1 5 10 15

Asp Val

<210> 78
 <211> 17
 <212> PRT
 <213> artificial sequence

<220>
 <223> sequence is synthesized

<220>
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 <222> 1-17
 <223> variant CDR sequence

<400> 78
 Tyr Pro His Tyr Tyr Ala His Glu Lys Lys Ser His Trp Tyr Phe
 1 5 10 15

Asp Val

<210> 79
 <211> 17
 <212> PRT
 <213> artificial sequence

<220>
 <223> sequence is synthesized

<220>
 <221> artificial
 <222> 1-17
 <223> variant CDR sequence

<400> 79
 Tyr Pro His Tyr Tyr Leu Lys Asp Arg Lys Ser His Trp Tyr Phe
 1 5 10 15

Asp Val

<210> 80
 <211> 17
 <212> PRT
 <213> artificial sequence

<220>
 <223> sequence is synthesized

<220>
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 <222> 1-17
 <223> variant CDR sequence

<400> 80
Tyr Pro His Tyr Tyr Gln His Asp Arg Thr Ser His Trp Tyr Phe
1 5 10 15

Asp Val

<210> 81
<211> 17
<212> PRT
<213> artificial sequence

<220>
<223> sequence is synthesized

<220>
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<222> 1-17
<223> variant CDR sequence

<400> 81
Tyr Pro His Tyr Tyr Val Thr Asp Arg Lys Ser His Trp Tyr Phe
1 5 10 15

Asp Val

<210> 82
<211> 17
<212> PRT
<213> artificial sequence

<220>
<223> sequence is synthesized

<220>
<221> artificial
<222> 1-17
<223> variant CDR sequence

<400> 82
Tyr Pro His Tyr Tyr Leu Arg Asp Lys Lys Ser His Trp Tyr Phe
1 5 10 15

Asp Val

<210> 83
<211> 17
<212> PRT
<213> artificial sequence

<220>
<223> sequence is synthesized

<220>
<221> artificial
<222> 1-17
<223> variant CDR sequence

<400> 83

Tyr Pro His Tyr Tyr Ser His Glu Arg Lys Ser His Trp Tyr Phe
 1 5 10 15

Asp Val

<210> 84
 <211> 17
 <212> PRT
 <213> artificial sequence

<220>
 <223> sequence is synthesized

<220>
 <221> artificial
 <222> 1-17
 <223> variant CDR sequence

<400> 84
 Tyr Pro His Tyr Tyr Leu Asn Glu Arg Lys Ser His Trp Tyr Phe
 1 5 10 15

Asp Val

<210> 85
 <211> 17
 <212> PRT
 <213> artificial sequence

<220>
 <223> sequence is synthesized

<220>
 <221> artificial
 <222> 1-17
 <223> variant CDR sequence

<400> 85
 Tyr Pro His Tyr Tyr Val Asn Glu Arg Lys Ser His Trp Tyr Phe
 1 5 10 15

Asp Val

<210> 86
 <211> 17
 <212> PRT
 <213> artificial sequence

<220>
 <223> sequence is synthesized

<220>
 <221> artificial
 <222> 1-17
 <223> variant CDR sequence

<400> 86
Tyr Pro His Tyr Tyr Leu Thr Asp His Lys Ser His Trp Tyr Phe
1 5 10 15

Asp Val

<210> 87
<211> 18
<212> PRT
<213> artificial sequence

<220>
<223> sequence is synthesized

<220>
<221> artificial
<222> 1-18
<223> variant CDR sequence

<400> 87
Tyr Pro His Tyr Tyr Leu Lys Asp Gly Lys Lys Ser His Trp Tyr
1 5 10 15

Phe Asp Val

<210> 88
<211> 17
<212> PRT
<213> artificial sequence

<220>
<223> sequence is synthesized

<220>
<221> artificial
<222> 1-17
<223> variant CDR sequence

<400> 88
Tyr Pro His Tyr Tyr Arg Arg Asp Lys Lys Ser His Trp Tyr Phe
1 5 10 15

Asp Val

<210> 89
<211> 17
<212> PRT
<213> artificial sequence

<220>
<223> sequence is synthesized

<220>
<221> artificial
<222> 1-17
<223> variant CDR sequence

<400> 89

Tyr Pro His Tyr Tyr Leu Lys Asp Lys Lys Ser His Trp Tyr Phe
 1 5 10 15

Asp Val

<210> 90
 <211> 17
 <212> PRT
 <213> artificial sequence

<220>
 <223> sequence is synthesized

<220>
 <221> artificial
 <222> 1-17
 <223> variant CDR sequence

<400> 90
 Tyr Pro His Tyr Tyr Leu His Asp Arg Lys Ser His Trp Tyr Phe
 1 5 10 15

Asp Val

<210> 91
 <211> 17
 <212> PRT
 <213> artificial sequence

<220>
 <223> sequence is synthesized

<220>
 <221> artificial
 <222> 1-17
 <223> variant CDR sequence

<400> 91
 Tyr Pro His Tyr Tyr Leu Ser Asp Lys Lys Ser His Trp Tyr Phe
 1 5 10 15

Asp Val

<210> 92
 <211> 17
 <212> PRT
 <213> artificial sequence

<220>
 <223> sequence is synthesized

<220>
 <221> artificial
 <222> 1-17
 <223> variant CDR sequence

<400> 92
 Tyr Pro His Tyr Tyr Val Asn Glu Arg Lys Ser His Trp Tyr Phe
 1 5 10 15

Asp Val

<210> 93
 <211> 45
 <212> DNA
 <213> artificial sequence

<220>
 <223> sequence is synthesized

<220>
 <221> artificial
 <222> 1-45
 <223> mutagenesis oligo

<400> 93
 taccgcgact attatgtgaa cgagcggaag agccactggt atttc 45

<210> 94
 <211> 110
 <212> PRT
 <213> artificial sequence

<220>
 <223> sequence is synthesized

<220>
 <221> artificial
 <222> 1-110
 <223> humanized antibody light chain variable domain

<400> 94
 Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val
 1 5 10 15

 Gly Asp Arg Val Thr Ile Thr Cys Ser Ala Ser Gln Asp Ile Ser
 20 25 30

 Asn Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys
 35 40 45

 Val Leu Ile Tyr Phe Thr Ser Ser Leu His Ser Gly Val Pro Ser
 50 55 60

 Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
 65 70 75

 Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln
 80 85 90

 Tyr Ser Thr Val Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu
 95 100 105

 Ile Lys Arg Thr Val
 110

<210> 95
 <211> 110
 <212> PRT
 <213> artificial sequence

<220>
 <223> sequence is synthesized

<220>
 <221> artificial
 <222> 1-110
 <223> humanized antibody light chain variable domain

<400> 95
 Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val
 1 5 10 15
 Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Asn Glu Gln Leu Ser
 20 25 30
 Asn Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys
 35 40 45
 Val Leu Ile Tyr Phe Thr Ser Ser Leu His Ser Gly Val Pro Ser
 50 55 60
 Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
 65 70 75
 Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln
 80 85 90
 Tyr Ser Thr Val Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu
 95 100 105
 Ile Lys Arg Thr Val
 110

<210> 96
 <211> 118
 <212> PRT
 <213> artificial sequence

<220>
 <223> sequence is synthesized

<220>
 <221> artificial
 <222> 1-118
 <223> humanized antibody heavy chain variable domain

<400> 96
 Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly
 1 5 10 15
 Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Thr Phe Thr
 20 25 30
 Asn Tyr Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
 35 40 45

Glu	Trp	Val	Gly	Trp	Ile	Asn	Thr	Tyr	Thr	Gly	Glu	Pro	Thr	Tyr	50	55	60
Ala	Ala	Asp	Phe	Lys	Arg	Arg	Phe	Thr	Phe	Ser	Leu	Asp	Thr	Ser	65	70	75
Lys	Ser	Thr	Ala	Tyr	Leu	Gln	Met	Asn	Ser	Leu	Arg	Ala	Glu	Asp	80	85	90
Thr	Ala	Val	Tyr	Tyr	Cys	Ala	Lys	Tyr	Pro	His	Tyr	Tyr	Gly	Ser	95	100	105
Ser	His	Trp	Tyr	Phe	Asp	Val	Trp	Gly	Gln	Gly	Thr	Leu			110	115	

<210> 97

<211> 118

<212> PRT

<213> artificial sequence

<220>

<223> sequence is synthesized

<220>

<221> artificial

<222> 1-118

<223> humanized antibody heavy chain variable domain

<400> 97

Glu	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Leu	Val	Gln	Pro	Gly	1	5	10	15
Gly	Ser	Leu	Arg	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Tyr	Asp	Phe	Thr	20	25	30	
His	Tyr	Gly	Met	Asn	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu	35	40	45	
Glu	Trp	Val	Gly	Trp	Ile	Asn	Thr	Tyr	Thr	Gly	Glu	Pro	Thr	Tyr	50	55	60	
Ala	Ala	Asp	Phe	Lys	Arg	Arg	Phe	Thr	Phe	Ser	Leu	Asp	Thr	Ser	65	70	75	
Lys	Ser	Thr	Ala	Tyr	Leu	Gln	Met	Asn	Ser	Leu	Arg	Ala	Glu	Asp	80	85	90	
Thr	Ala	Val	Tyr	Tyr	Cys	Ala	Lys	Tyr	Pro	His	Tyr	Tyr	Gly	Ser	95	100	105	
Ser	His	Trp	Tyr	Phe	Asp	Val	Trp	Gly	Gln	Gly	Thr	Leu			110	115		

<210> 98

<211> 121

<212> PRT

<213> artificial sequence

<220>

<223> sequence is synthesized

<220>
 <221> artificial
 <222> 1-121
 <223> humanized antibody heavy chain variable domain

<400> 98

Glu	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Leu	Val	Gln	Pro	Gly
1				5					10					15
Gly	Ser	Leu	Arg	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Tyr	Thr	Phe	Thr
				20					25					30
Asn	Tyr	Gly	Met	Asn	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu
				35					40					45
Glu	Trp	Val	Gly	Trp	Ile	Asn	Thr	Tyr	Thr	Gly	Glu	Pro	Thr	Tyr
				50					55					60
Ala	Ala	Asp	Phe	Lys	Arg	Arg	Phe	Thr	Phe	Ser	Leu	Asp	Thr	Ser
				65					70					75
Lys	Ser	Thr	Ala	Tyr	Leu	Gln	Met	Asn	Ser	Leu	Arg	Ala	Glu	Asp
				80					85					90
Thr	Ala	Val	Tyr	Tyr	Cys	Ala	Lys	Tyr	Pro	His	Tyr	Tyr	Val	Asn
				95					100					105
Glu	Arg	Lys	Ser	His	Trp	Tyr	Phe	Asp	Val	Trp	Gly	Gln	Gly	Thr
				110					115					120

Leu

<210> 99
 <211> 121
 <212> PRT
 <213> artificial sequence

<220>
 <223> sequence is synthesized

<220>
 <221> artificial
 <222> 1-121
 <223> humanized antibody heavy chain variable domain

<400> 99

Glu	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Leu	Val	Gln	Pro	Gly
1				5					10					15
Gly	Ser	Leu	Arg	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Tyr	Asp	Phe	Thr
				20					25					30
His	Tyr	Gly	Met	Asn	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu
				35					40					45
Glu	Trp	Val	Gly	Trp	Ile	Asn	Thr	Tyr	Thr	Gly	Glu	Pro	Thr	Tyr
				50					55					60
Ala	Ala	Asp	Phe	Lys	Arg	Arg	Phe	Thr	Phe	Ser	Leu	Asp	Thr	Ser
				65					70					75

Lys Ser Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp
80 85 90

Thr Ala Val Tyr Tyr Cys Ala Lys Tyr Pro His Tyr Tyr Val Asn
95 100 105

Glu Arg Lys Ser His Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr
110 115 120

Leu